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| 09/833,745 | 04/13/2001 | Joseph Roberts | 78728/106 | 2894 |

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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

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| EXAMINER |
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PATTERSON, CHARLES L JR

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| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 03/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Supplemental
Office Action Summary

Application No.

09/833,745

Applicant(s)

ROBERTS ET AL.

Examiner

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/18/01, 8/9/01, 5/10/02 and 8/29/02.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 and 21-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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The examiner mistakenly examined groups I-VI, claims 1-6, even though applicants elected group VII, claims 7-20 in Paper No. 10. Accordingly another action is done herewith that supercedes the previous action mailed 11/5/02, Paper No. 11. This action completely replaces the previous action.

Applicant's election with traverse of claims 7-20 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that Groups I-V all encompass SEQ ID NO:1, with the other groups claiming expanded regions, Group VI also comprises SEQ ID NO:1 and highlights variations and further that there must be a serious burden upon the examiner. Applicants also argue that "the product as claimed can be used in a materially different process" and "[i]t is the enzymatic activity of the polypeptide [of Groups I-VI] that makes it an effective therapeutic...[and] the therapeutic capability...cannot be divorced from the enzyme's activity". They further argue that "separate status of the art may be shown by citing patents" and that Groups V-VI fall within one class (435) and subclass (232)...[and that] Groups VII and VIII also fall within the same class (435)". This is not found persuasive because Group VI apparently is a structurally different product from Groups I-V; even though the enzymatic activity is what is the therapeutic use, the enzyme could be used for other purposes such as its enzymatic activity not related to treatment; though some of the groups are classified in the same class, they are not classified in the same subclass. In this regard it is noted that there is a typographical error in the classification of Group VII, which should be class 424, subclass 94.1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6 and 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no

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allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

The disclosure is objected to because of the following informalities:

In addition to the objection to the drawings shown on the enclosed PTO-948, the examiner objects to Figures 5 and 6. The numbers shown at the top of the figures do not line up with the lanes on the gel.

In paragraph 36, Figure 10 is stated as depicting the effectiveness of L-histidinol as a single agent and in combination with HAL. The instant figure apparently only shows the effect of L-histidinol alone, not with HAL.

In the amendment filed 7/15/01, it is requested that paragraph 00127 be substituted for. Apparently the correct paragraph is 00128. The examiner has made an attempt to change the entry of the instant amendment but the red ink used was permanent. The simplest way to remedy this is to delete what was in the previous amendment and substitute paragraphs 00127 and 00128.

In the amendment filed 7/18/01 changing the description of Figure 14, the sequences are disclosed as "43-64, respectively". This is 22 sequences and there are only 21 sequences in the figure.

In the same amendment, Table 1 is indicated as including SEQ ID NO:1-27, while there are only 19 sequences in the table. Also, "coordinates" in Table 1 apparently is meant to refer to the residue positions. This is not understood as e.g. SEQ ID NO:1 has 37 residues (amino acids) but the "coordinates" for the first sequence in Table 1 are 838-867. Also, SEQ ID NO:1-6 and 8-11 are amino acid sequences, not nucleotide sequences as shown in Table 1.

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In paragraph 133 it is stated that the data from the sequence analysis of the 55 kDa protein is shown in Figure 2. Figure 2 only shows 3 short sequences, so it does not show the data from the sequencing.

In paragraph 146, line 4, it is stated that "below is a graph". No graph is seen below.

Appropriate correction is required.

Claims 10, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite in the recitation of "a patient in need of treatment". Who is such a patient? How is such a patient determined? From what is such a patient suffering?

Claim 12 is confusing in that it depends upon a claim that was not elected for prosecution.

Claim 13 is indefinite in the recitation of "and administering to said patient... a chemotherapeutic agent". It is not clear from the language of the claim whether the chemotherapeutic agent is in addition to the lyase or if it is the same agent. A recitation of "and also [or additionally] administering to said patient... a chemotherapeutic agent" would overcome this rejection.

Claims 7-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or

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use the invention. This is a combination written description and enablement rejection.

The specification teaches that the histidine ammonia lyase from *Corynebacteriaceae* is relatively resistant to L-histidinol (HAL) and will inhibit the production of some viruses and will do this even better in the presence of L-histidinol. It does not show the effect of using HAL with other histidine analogs. HAL has also been shown to inhibit the growth of certain cancer cell lines. However, other histidine ammonia lyases have not been shown to have these effects, nor has HAL or any other histidine ammonia lyase been shown to deliver an immunosuppressant to a patient as in claims 16-20. None of the instant claims are limited to the embodiments discussed and therefore it is maintained that one of ordinary skill in the art would not believe that applicants had possession of the claimed invention when the application was filed. Also, one of ordinary skill in the art would not be taught by the instant specification how to make and/or use invention within the scope of the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Roberts, et al. (A1) or Jack, et al. (A5). The two references teach the treatment of tumors with histidase. Reference is made to the 35

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USC § 112 second paragraph rejection *supra* where it is stated that claim 13 is not clear as to whether the lyase is the chemotherapeutic agent or whether it is intended to claim an additional chemotherapeutic agent. The amount that is therapeutic could have been determined by trial and error. It is not known whether the non-diseased cells enter a reversible quiescent state but absent convincing proof to the contrary it is maintained that this is inherent. The motivation would have been to treat disease.


Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts, et al. (A1) or Jack, et al. (A5) in view of either of Shittigar (A) or Kinstler, et al. (B). Roberts, et al. and Jack, et al. have been characterized *supra*. Shittigar teaches in the paragraph spanning columns 2-3 that polyethylene glycol increases the biological half life and reduces the immunogenicity of an enzyme. Kinstler, et al. teach in column 1, lines 34-55 that polyethylene glycol protects enzymes from proteolysis. It would have been obvious to one of ordinary skill in the art to use polyethylene glycol (PEGylation) on the enzyme taught by Roberts, et al. or Jack, et al., absent unexpected results. The motivation would have been to protect against proteolysis, increase half life and/or reduce the immunogenicity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
February 25, 2003